

haloalkyl), $-\text{SO}_2\text{NH}_2$, $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2\text{NH}(\text{phenyl})$, $-\text{NHSO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{NHSO}_2(\text{phenyl})$, and $-\text{NHSO}_2(\text{C}_1\text{-C}_4 \text{ haloalkyl})$.

[0066] Antimitotic refers to a drug for inhibiting or preventing mitosis, for example, by causing metaphase arrest. Some antitumour drugs block proliferation and are considered antimitotics.

[0067] Aryl and heteroaryl mean a 5- or 6-membered aromatic or heteroaromatic ring containing 0 or 1-4 heteroatoms, respectively, selected from O, N, or S; a bicyclic 9- or 10-membered aromatic or heteroaromatic ring system containing 0 or 1-4 (or more) heteroatoms, respectively, selected from O, N, or S; or a tricyclic 12- to 14-membered aromatic or heteroaromatic ring system containing 0 or 1-4 (or more) heteroatoms, respectively, selected from O, N, or S. The aromatic 6- to 14-membered carbocyclic rings include, e.g., phenyl, naphthyl, indanyl, tetralinyl, and fluorenyl and the 5- to 10-membered aromatic heterocyclic rings include, e.g., imidazolyl, pyridinyl, indolyl, thienyl, benzopyranonyl, thiazolyl, furanyl, benzimidazolyl, quinolinyl, isoquinolinyl, quinoxalinyl, pyrimidinyl, pyrazinyl, tetrazolyl and pyrazolyl.

[0068] Aralkyl- refers to a residue in which an aryl moiety is attached to the parent structure via an alkyl residue. Examples include benzyl, phenethyl, phenylvinyl, phenylallyl and the like. Heteroaralkyl- refers to a residue in which a heteroaryl moiety is attached to the parent structure via an alkyl residue. Examples include furanylmethyl, pyridinylmethyl, pyrimidinylethyl and the like.

[0069] Aralkoxy- refers to the group $-\text{O}$ -aralkyl. Similarly, heteroaralkoxy- refers to the group $-\text{O}$ -heteroaralkyl; aryloxy- refers to the group $-\text{O}$ -aryl; acyloxy- refers to the group $-\text{O}$ -acyl; heteroaryloxy- refers to the group $-\text{O}$ -heteroaryl; and heterocyclyloxy- refers to the group $-\text{O}$ -heterocyclyl (i.e., aralkyl, heteroaralkyl, aryl, acyl, heterocyclyl, or heteroaryl is attached to the parent structure through an oxygen).

[0070] Carboxyalkyl- refers to the group $-\text{alkyl-COOH}$.

[0071] Carboxamido refers to the group $-\text{CONR}^b\text{R}^c$, where

[0072] R^b is H or optionally substituted $\text{C}_1\text{-C}_6$ alkyl, aryl, heteroaryl, aryl- $\text{C}_1\text{-C}_4$ alkyl-, or heteroaryl- $\text{C}_1\text{-C}_4$ alkyl- group; and

[0073] R^c is hydrogen or $\text{C}_1\text{-C}_4$ alkyl; and

[0074] where each optionally substituted R^b group is independently unsubstituted or substituted with one or more substituents independently selected from $\text{C}_1\text{-C}_4$ alkyl, aryl, heteroaryl, aryl- $\text{C}_1\text{-C}_4$ alkyl-, heteroaryl- $\text{C}_1\text{-C}_4$ alkyl-, $\text{C}_1\text{-C}_4$ haloalkyl, $-\text{OC}_1\text{-C}_4$ alkyl, $-\text{OC}_1\text{-C}_4$ alkylphenyl, $-\text{C}_1\text{-C}_4$ alkyl-OH, $-\text{OC}_1\text{-C}_4$ haloalkyl, halogen, $-\text{OH}$, $-\text{NH}_2$, $-\text{C}_1\text{-C}_4$ alkyl- NH_2 , $-\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkylphenyl})$, $-\text{NH}(\text{C}_1\text{-C}_4 \text{ alkylphenyl})$, cyano, nitro, oxo (as a substituent for heteroaryl), $-\text{CO}_2\text{H}$, $-\text{C}(\text{O})\text{OC}_1\text{-C}_4$ alkyl, $-\text{CON}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CONH}_2$, $-\text{NHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{NHC}(\text{O})(\text{phenyl})$, $-\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})\text{C}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})\text{C}(\text{O})(\text{phenyl})$, $-\text{C}(\text{O})\text{C}_1\text{-C}_4$ alkyl, $-\text{C}(\text{O})\text{C}_1\text{-C}_4$ phenyl, $-\text{C}(\text{O})\text{C}_1\text{-C}_4$ haloalkyl, $-\text{OC}(\text{O})\text{C}_1\text{-C}_4$ alkyl,

$-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2(\text{phenyl})$, $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ haloalkyl})$, $-\text{SO}_2\text{NH}_2$, $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2\text{NH}(\text{phenyl})$, $-\text{NHSO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{NHSO}_2(\text{phenyl})$, and $-\text{NHSO}_2(\text{C}_1\text{-C}_4 \text{ haloalkyl})$.

[0075] Halogen or halo refers to fluorine, chlorine, bromine or iodine. Fluorine, chlorine and bromine are preferred. Dihaloaryl, dihaloalkyl, trihaloaryl etc. refer to aryl and alkyl substituted with the designated plurality of halogens (here, 2, 2 and 3, respectively), but not necessarily a plurality of the same halogen; thus 4-chloro-3-fluorophenyl is within the scope of dihaloaryl.

[0076] Heterocyclyl means a cycloalkyl or aryl residue in which one to four of the carbons is replaced by a heteroatom such as oxygen, nitrogen or sulfur. Examples of heterocycles that fall within the scope of the invention include azetidiny, imidazoliny, pyrrolidiny, pyrazolyl, pyrrolyl, indolyl, quinolinyl, isoquinolinyl, tetrahydroisoquinolinyl, benzofuranyl, benzodioxanyl, benzodioxyl (commonly referred to as methylenedioxypheyl, when occurring as a substituent), tetrazolyl, morpholinyl, thiazolyl, pyridinyl, pyridazinyl, piperidinyl, pyrimidinyl, thienyl, furanyl, oxazolyl, oxazolinyl, isoxazolyl, dioxanyl, tetrahydrofuranyl and the like. "N-heterocyclyl" refers to a nitrogen-containing heterocycle. The term heterocyclyl encompasses heteroaryl, which is a subset of heterocyclyl. Examples of N-heterocyclyl residues include azetidiny, 4-morpholinyl, 4-thiomorpholinyl, 1-piperidinyl, 1-pyrrolidinyl, 3-thiazolidinyl, piperazinyl and 4-(3,4-dihydrobenzoxazinyl). Examples of substituted heterocyclyl include 4-methyl-1-piperazinyl and 4-benzyl-1-piperidinyl.

[0077] A leaving group or atom is any group or atom that will, under the reaction conditions, cleave from the starting material, thus promoting reaction at a specified site. Suitable examples of such groups unless otherwise specified are halogen atoms, mesyloxy, p-nitrobenzensulphonyloxy and tosyloxy groups.

[0078] Optional or optionally means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstances occurs and instances in which it does not. For example, "optionally substituted alkyl" includes "alkyl" and "substituted alkyl" as defined herein. It will be understood by those skilled in the art with respect to any group containing one or more substituents that such groups are not intended to introduce any substitution or substitution patterns that are sterically impractical and/or synthetically non-feasible and/or inherently unstable.

[0079] Substituted alkoxy refers to alkoxy wherein the alkyl constituent is substituted (i.e., $-\text{O}$ -(Substituted alkyl)). One preferred substituted alkoxy group is "polyalkoxy" or $-\text{O}$ -(optionally substituted alkylene)-(optionally substituted alkoxy), and includes groups such as $-\text{OCH}_2\text{CH}_2\text{OCH}_3$, and residues of glycol ethers such as polyethyleneglycol, and $-\text{O}(\text{CH}_2)_x\text{CH}_2\text{OCH}_3$, where x is an integer of about 2-20, preferably about 2-10, and more preferably about 2-5. Another preferred substituted alkoxy group is hydroxyalkoxy or $-\text{OCH}_2(\text{CH}_2)_y\text{OH}$, where y is an integer of about 1-10, preferably about 1-4.

[0080] Substituted- alkyl, aryl, and heteroaryl, which includes the substituted alkyl, aryl and heteroaryl moieties of any group containing an optionally substituted alkyl, aryl